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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/668,564	09/23/2003	Nicholas Michael Morton	674543-2004	3906

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EXAMINER	
MCMILLIAN, KARA RENITA	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,564	MORTON ET AL.	
	Examiner	Art Unit	
	KARA R. MCMILLIAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 18-53* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 27-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,18-26,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment received on March 20, 2008 has been entered. Applicants have withdrawn claims 1-13 and 27-51, cancelled claims 15-17, amended claims 14 and 18-23, and added claims 52-53.

Claims 14, 18-26, and 52-53 are currently pending.

Response to Arguments

In view of Applicant's amendments to claims 20, 22, and 23, the rejection of said claims under 35 USC § 112 second paragraph is hereby withdrawn.

Upon further consideration, the previous rejections under 35 USC § 102(b) and 35 USC § 103 in the office action sent out on September 20, 2007 are hereby withdrawn. Applicants arguments with respect to claims 14-26 under 35 USC § 102(b) and 35 USC § 103 were considered but are now moot in view of the withdrawal of the rejections.

In response to Applicant's recent amendments to the claims submitted on March 20, 2008 the following rejections apply:

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United Kingdom on March 23, 2001. It is noted, however, that

applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 53 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmacologically downregulating the production of the 11β-HSD1 protein from the mRNA, does not reasonably provide enablement for the pharmacological prevention of the production of the 11β-HSD1 protein from the mRNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention

commensurate in scope with these claims. The specification does not provide sufficient information to show the pharmacological prevention of 11β-HSD1 protein synthesis.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art, the relative skill of those in the art, and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: Claim 53 of the instant application claims a method for reducing cardiovascular disease risk in an animal comprising the administration of an agent that prevents or downregulates 11β-HSD1 protein synthesis.

Breadth of the claims: The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The rejected claim is extremely broad. Applicants claim that not only can 11β-HSD1 protein synthesis be downregulated but prevented as well. For purposes of patent examination, prevention is interpreted as all or none, i.e. either all protein synthesis is inhibited or it is not. Thus if protein synthesis is pharmacologically prevented, there would be no 11β-HSD1 protein activity since there would be no 11β-HSD1 protein produced from the mRNA.

Guidance of the Specification/Working Examples: Applicants have only provided data showing that carbenoxolone and other similarly acting steroids reduce the activity of 11β-HSD1.

State of the Art: At the time of the instant invention pharmacological agents such as steroids were known to reduce the activity of 11β-HSD1 (Monder et al. 1993). Diederich et al. (2000, provided on IDS dated 3/25/04) also reported that certain agents such as progesterone inhibit 11β-HSD1 activity and that chenodeoxycholic acid selectively inhibits 11β-HSD1 activity (see Table 1 on page 203). In addition, Hermanowski-Vosatka et al. (2000, provided on IDS dated 3/25/08) showed that PPARα agonists such as fenofibrate also reduce 11β-HSD1 protein expression. These studies do not show that these agents are capable of preventing 11β-HSD1 protein expression.

Predictability/Unpredictability in the Art: There is a general lack of predictability in the pharmaceutical art. In re Fisher, 427, F. 2d 833, 166, USPQ 18 (CCPA 1970). It would be unpredictable for the skilled artisan to reduce cardiovascular disease risk by administrating an agent that prevents 11β-HSD1 protein synthesis since prevention of 11β-HSD1 protein synthesis is not known in the art and the instant specification does not provide suitable guidance and examples for the prevention of 11β-HSD1 protein synthesis.

The Quantitation of Experimentation Required: In order to practice Applicants invention, it would be necessary for one to conduct an exhaustive amount of

experiments. Applicant would need to provide reasonable data showing that pharmacological agents can prevent 11β-HSD1 protein synthesis. Therefore, in order to practice the claimed invention, the amount of experimentation required would be considered undue and burdensome.

In conclusion, Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague limitations of general ideas that may or may not be workable." A method for reducing cardiovascular disease risk in an animal comprising the administration of an agent that prevents 11β-HSD1 protein synthesis is not enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 18, referring to Table IV of Monder C, and White PC, Vitamins and Hormones 1993: 47:187-271 renders said claim indefinite since said claim does not stand alone. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14,18-23, and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Levine et al. U.S. Patent No. 5,985,861 as evidenced by Monder et al., 1993, Vitamins and Hormones, 47:187-271.

Claims 14,18-23, and 52 of the instant application claim a method for reducing cardiovascular disease risk in an animal at risk comprising administering a pharmaceutically effective amount of an agent which directly inhibits 11β-HSD1 protein synthesis or activity such as steroids.

Levine et al. discloses a method of treating or reducing ischemia or the incidence of cardiovascular events or treating coronary artery disease comprising the administration of progesterone (see abstract and column 1 line 66 through column 2 line 3). Table IV of Monder et al. identifies progesterone as a steroid capable of inhibiting 11β-HSD1 activity (see page 196). Furthermore claim 18 of the instant application claims a method for reducing cardiovascular disease risk in an animal at risk comprising administering a pharmaceutically effective amount of an agent which directly inhibits 11β-HSD1 protein synthesis or activity wherein said agent is selected from the steroids listed on Table IV of Monder et al. As such claims 14,18, and 52 are anticipated by Levine et al. as evidenced by Monder et al.

Claims 19-23 are also anticipated by Levine et al. as evidenced by Monder et al. since Levine et al. claims a reduction in the incidence of cardiovascular events by the administration of progesterone and progesterone inhibits 11β-HSD1 activity. The properties claimed in claims 19-23 of the instant application are inherent properties of progesterone since progesterone reduces the incidence of cardiovascular events and inhibits 11β-HSD1 activity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al. U.S. Patent No. 5,985,861 as evidenced by Monder et al., 1993, Vitamins and Hormones, 47:187-271.

Claim 53 of the instant application claims a method for reducing cardiovascular disease risk in an animal comprising the administration of an agent that prevents or downregulates 11β-HSD1 protein synthesis.

Levine et al. as evidenced by Monder et al. is as set forth above.

Levine et al. as evidenced by Monder et al. does not specifically teach that progesterone downregulates the production of the 11β-HSD1 protein from 11β-HSD1 mRNA.

Monder et al. teaches that progesterone inhibits the activity of 11β-HSD1 thus all the ways in which the activity of a protein can be inhibited (i.e. decrease the message (mRNA) or increase protein degradation, etc.) are contemplated. It is incumbent upon Applicant to demonstrate the criticality of said limitation of instant claim 53.

Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al. U.S. Patent No. 5,985,861 as evidenced by Monder et al., 1993, Vitamins and Hormones, 47:187-271 as applied to claims 14,18-23, and 52-53 above and further in view of Kotelevtsev et al. 1997, PNAS, 94:14924-14929 (provided on IDS dated 3/25/04).

Claims 24-25 of the instant application claim the method of instant claim 14 wherein the agent increases insulin sensitivity risk and improves glucose tolerance in an animal at risk of cardiovascular disease.

Levine et al. as evidenced by Monder et al. anticipates instant claim 14 as described above. Levine et al. does not teach that progesterone increases insulin sensitivity risk or improves glucose tolerance in an animal at risk of cardiovascular disease.

Kotelevtsev et al. teaches that animals without 11β-HSD1 are resistant to the induction of hyperglycemia produced by diet as compare to animals that express 11β-HSD1 (see abstract and page 14927). Based on said disclosure of Kotelevtsev et al. it would be obvious to one of ordinary skill in the art that downregulation of 11β-HSD1

would improve glucose tolerance and increase insulin sensitivity since animals 11β-HSD1 null were resistant to hyperglycemia.

Since Monder et al. teaches that progesterone decreases 11β-HSD1 activity and Kotelevtsev et al. obviates that downregulation of 11β-HSD1 activity improves glucose tolerance and increase insulin sensitivity, progesterone would necessarily improve glucose tolerance and increase insulin sensitivity. As such claims 24-25 are rendered obvious in view of Levine et al. (as evidenced by Monder et al.) and further in view of Kotelevtsev et al.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Levine et al. U.S. Patent No. 5,985,861 as evidenced by Monder et al., 1993, Vitamins and Hormones, 47:187-271 in view of Kotelevtsev et al. 1997, PNAS, 94:14924-14929 as applied to claims 24-25 above and further in view of Fruchart et al. 1999, Current Opinion in Lipidology, 10(3):245-257.

Levine et al. as evidenced by Monder et al. in view of Kotelevtsev et al. 1997, as applied to claims 14 and 18-25 is as set forth above.

Levine et al. (as evidenced by Monder et al.) in view of Kotelevtsev et al. does not disclose the use of a PPARα agonist in conjunction with an agent that reduces 11β-HSD1 activity in a method for the promotion of an atheroprotective lipid profile.

Fruchart et al. teaches that PPARα activators such as fibrates (e.g. fenofibrate) inhibit the development of atherosclerosis through their normolipidemic activities as well

as through inhibition of vascular inflammation and thrombogenesis (see abstract and conclusion on page 254).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Levine et al. which teaches a method for treating or reducing ischemia or the incidence of cardiovascular events or treating coronary artery disease comprising the administration of progesterone (see abstract and column 1 line 66 through column 2 line 3) with the teachings of Fruchart et al. which teaches that fibrates such as fenofibrate which are PPARα agonists inhibit the development of atherosclerosis through is ability to improve plasma lipid profile and decrease vascular wall inflammation (see abstract). An ordinary skilled artisan would be motivated to use both types of drugs in the treatment or reduction of atherosclerosis in order to produce an increased treatment outcome. The examiner respectfully points out the following from MPEP 2144.06:

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ....

[T]he idea of combining them flows logically from

their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850,205 USPQ 1069, 1072 (CCPA 1980).

As such claim 26 is rendered obvious in view of the recited prior art references.

Conclusions

Claims 14, 18-26, and 52-53 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARA R. MCMILLIAN whose telephone number is (571)270-5236. The examiner can normally be reached on Monday-Thursday from 8:30 am- 6:00 pm and every other Friday from 8:30 am- 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kara R. McMillian/
Examiner, Art Unit 1617

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